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Mutational analysis of the interaction between CD4 and class II MHC: class II antigens contact CD4 on a surface opposite the gp120-binding site.

Fleury S, Lamarre D, Meloche S, Ryu SE, Cantin C, Hendrickson WA, Sekaly RP.

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Using functional and adhesion assays, we have studied the ability of 30 human CD4 mutants to interact with class II major histocompatibility complex (MHC) molecules and also with gp120 from human immunodeficiency virus. The mutants cover the four domains (D1-D4) of CD4 and include several single-site substitutions. Analysis of the results, in the context of the CD4 crystal structure, shows that mutations that affect the interaction with class II MHC molecules are located on three exposed loops from CD4 domains 1 and 2. The specifically implicated residues, 19, 89, and 165, are separated from one another by 9 A, 24 A, and 24 A on one face of the CD4 molecule. Moreover, the class II binding site does not include residues 43 to 49 of the CD4 molecule, a region on an opposite face known to be involved in the binding of gp120.

PMID: 1889086 [PubMed - indexed for MEDLINE]

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